

The Determinants of Diphtheria Outbreak in Cirebon City

Mohamad Rahman Suhendri¹ Pariawan Lutfi Ghazali^{2,*}

¹ Faculty of Medicine, Universitas Islam Indonesia

² Department of Public Health, Faculty of Medicine, Universitas Islam Indonesia

*Corresponding author. Email: elghazali@uii.ac.id

ABSTRACT

Background: Indonesia's Ministry of Health reported 3,944 cases of diphtheria that occurred between 2011 and 2017 with 142 deaths. One of the cities with a high number of diphtheria cases is Cirebon. This study aimed to determine the factors related to diphtheria outbreaks in Cirebon. **Methods:** This observational study used a case-control design with a descriptive-analytic type. The total samples in this study were 33 with 11 case groups and 22 control groups. The independent variables consisted of age, nutritional status, immunization status, sex, and source of transmission. The sources of research data were medical records and questionnaires. The data were analyzed through univariate, bivariate, and multivariate analyses with $p = 0.05$. **Results:** The variables with a significant correlation with diphtheria were immunization status ($p = 0.009$), age (0.022), and source of transmission ($p = 0.033$). Meanwhile, nutritional status ($p = 0.721$) and sex ($p = 1,000$) were not related to diphtheria. The most influential variable was immunization status with 22.727 OR. The factors associated with unimmunized individuals or incomplete immunizations were low levels of education, poor knowledge, poverty, misconceptions, and certain religious beliefs in which immunization is not allowed. **Conclusion:** The factors related to diphtheria incidence are immunization status (the most dominant factor), age, and source of transmission.

Keywords: Determinant, Diphtheria, Outbreak

1. INTRODUCTION

Diphtheria is an acute disease caused by *Corynebacterium Diphtheriae* toxin. It attacks the upper respiratory tract, including tonsil, nasal, and throat[1]. *Corynebacterium Diphtheriae* toxin can inhibit protein synthesis, damage the locally affected tissue, and form a pseudomembrane[2]. Moreover, once the toxin reaches the blood vessels, it may lead to myocarditis, neuritis, thrombocytopenia, and proteinuria[1] [2].

This is a scarce disease of which prevalence is therefore quite low. According to the Law of Indonesia's Ministry of Health No. 948 of 2004, diphtheria is categorized as an outbreak. Indonesia suffered from diphtheria outbreaks from 1997 to 2002 in Jambi, Lampung, Bengkulu, South Sumatra, South Kalimantan, Central Kalimantan, East Kalimantan, South Sulawesi, North Sulawesi, Bali, West Java, Central Java, Special Region of Yogyakarta, and East Java[3]. Over the past 6 years (2011-2017), there were 3,944 diphtheria cases reported, and 142 of the sufferers died. This has placed Indonesia in the second position among countries with the most diphtheria cases in the world after India[4][5]. Indonesia's Ministry of Health stated that during 2017 diphtheria outbreak occurred in 170 regencies/cities and 30 provinces with a total of 954 cases and 44 deaths [6]. Meanwhile, Cirebon is one of the towns in West Java in which the number of diphtheria cases is reasonably high, reaching 16 cases in 2016 and 6 cases in 2017[7].

This study aims to investigate the factors that correlate with the diphtheria outbreak in Cirebon. The results of this study can be taken into account when establishing a government policy and become a reference to educate the society.

2. METHODS

This was an observational study with a case-control design. Data collection was conducted in Cirebon in April and May 2018. The cases involved in this study were 11 cases recorded in the Cirebon Health Office data over the period of 2016-2018 of which residences are currently being tracked. The number of subjects in the control group was 22, determined using the formula $2n$, $3n$, $4n$, etc. where n is the number of cases[8]. The determinants of diphtheria included in this study were age, vaccination status, source of transmission, sex, and nutritional status.

The main data was obtained through interviews and direct measurement, while the secondary data was collected from the medical records in Gunung Jati Public Hospital and the epidemiology data in Cirebon Health Office. These data were then analyzed using bivariate and multivariate techniques.

3. RESULTS

The distribution of diphtheria cases in Cirebon town during 2016 – 2018 was shown in 10 different sub-districts. Most of the cases occurred in Pegambiran sub-district with 8 cases while the other 9 sub-districts had only 1 – 2 cases.

Based on the bivariate analysis, sex did not have a significant correlation with the incidence of diphtheria, as shown in Table 1. The proportion of male and female in the diphtheria cases was equal (50%).

The bivariate analysis also found that vaccination status had a significant correlation with the incidence of diphtheria (p value=0.009), as described in Table 2.

Another variable which significantly correlated with diphtheria incidence was the transmission sources (p value=0.033), as pictured in Table 3.

Nutritional status has a mutual correlation with infection incidence [9], including diphtheria. However, the bivariate analysis in this study found that nutritional status had no significant correlation with diphtheria incidence (p=0.721), as framed in Table 4.

The bivariate analysis has shown that the risk age group had a significant correlation with diphtheria incidence, as shown in Table 5.

The variables that can be analyzed are those with a p-value of <0.25[8]. In this research, they included the source of transmission, vaccination status, and age status. All variables with p-value > 0.1 were excluded from the analysis one by one, starting from the one with the largest p-value. The multivariate analysis is shown in Table 6 and Table 7.

Table 1. The correlation between sex and diphtheria incidence

Sex	Case		Control		Total		OR	p value
	Σ	%	Σ	%	Σ	%		
Male	6	54	12	54	18	54	1	1.000
Female	5	46	10	46	15	46		
Total	11	100	22	100	33	100	95% CI =0.234-4.278	

Table 2. The correlation between vaccination status and diphtheria incidence

Vaccination Status	Case		Control		Total		OR	p value
	Σ	%	Σ	%	Σ	%		
Incomplete	10	90	9	40	19	57	14.44	0.009
Complete	1	10	13	60	14	43		
Total	11	100	22	100	33	100	95% CI =1.562-133.580	

Table 3. The correlation between transmission sources and diphtheria incidence

Transmission Sources	Case		Control		Total		OR	p value
	Σ	%	Σ	%	Σ	%		
Yes	5	45	19	86	24	72	0.132	0.033
No	6	55	3	14	9	28		
Total	11	100	22	100	33	100	95% CI =0.024-0.721	

Table 4. The correlation between nutritional status and diphtheria incidence

Nutritional Status	Case		Control		Total		OR	p value
	Σ	%	Σ	%	Σ	%		
Abnormal	5	46	11	50	16	49	0.694	0.721
Normal	6	54	11	50	17	51		
Total	11	100	22	100	33	100	95% CI =0.162-2.971	

Table 5. The correlation between age and diphtheria incidence

Age group	Case		Control		Total		OR	p value
	Σ	%	Σ	%	Σ	%		
Risk Age Group	10	90	10	45	20	60	12	0.022
No-Risk Age Group	1	10	12	55	13	40		
Total	11	100	22	100	33	100	95% CI =1.303-110.525	

Table 6. Multivariate model 1

Variable	B	P value	Exp B	95% CI
Transmission Source	2.428	0.044	11.333	1.071-119.875
Vaccination Status	-2.608	0.101	0.074	0.03-1.665
Age Status	-0.824	0.564	0.439	0.027-7.190

Constant = 1.451

Table 7. Multivariate model 2

Variable	B	P value	Exp B	95% CI
Transmission Source	2.539	0.033	12.662	1.230-130.339
Vaccination Status	-3.117	0.022	0.044	0.003-0.638

Constant = 1.137

4. DISCUSSION

Pegambiran sub-district, as the area with the most diphtheria incidence in Cirebon, is located on the north coast of Cirebon. This is a slum area where the distance between houses is close, and a large amount of garbage and numerous puddles can be found on every corner. The close distance among the houses enables pathogen transmission to occur easily through either direct contact or airborne transmission[5], [9]. Another study claimed that a dense dwelling is significantly correlated with the incidence of diphtheria with p-value < 0.003[10].

However, sex is not linked to diphtheria incidence. This is similar to the previous studies which clarified that there is no correlation between sex and diphtheria incidence [10]–[12].

The human immune system consists of two types of immunity, namely non-specific immunity and specific immunity[10]. Non-specific immunity is an immune system that normally works in all conditions. However, this system is less adequate against specific pathogens, such as diphtheria[5], [10]. The human body requires particular preparation to deal with diphtheria through DTaP vaccine. In most cases, diphtheria occurs to unvaccinated individuals[5]. A group with incomplete vaccination status has 14.44 times more risk of contracting diphtheria compared to that having complete vaccination status. The

spatial data analysis of East Java in 2010 – 2011 clarified that the area with low DTaP and Tdap vaccination has a significantly high number of diphtheria cases.[13]. Some other studies claimed that incomplete vaccination has 3.9 times[14], 46.403 times[9], and 2.74 times[15] higher risk of making individuals infected by diphtheria as opposed to complete vaccination. Cirebon is one of the towns in West Java with low DTaP vaccination coverage, reaching only 87%[16].

Immunization process is not only about the shot but also a matter of vaccine quality. The quality of a vaccine is determined by the production, distribution, storage, and administration methods[10]. A common issue that reduces the quality of vaccine in Indonesia is the cold chain management[5]. It may include electrical disturbance and/or vaccine storage that is mixed with food in the refrigerator. The temperature in the refrigerator is unstable since the door is frequently opened and closed [17].

Surprisingly, the transmission source indicates an inverse correlation ($OR=0.132$) in which those with no transmission sources have a higher possibility to suffer from diphtheria. This may happen due to selection and information bias during the data collection which is difficult to control. Other studies showed a positive correlation between source of transmission and diphtheria incidence, with an odds ratio of 3.5[12] and 22.821[10]. Transmission source is considered as a diphtheria determinant since diphtheria bacteria can spread in the air which has been contaminated by a patient's cough, sneeze, or sputum[1]. A transmission source in an area is able to accelerate pathogen transmission among residences[9].

Nutrition is an issue linked to nearly all infectious diseases[5]. The existence of nutrition problem is mainly associated with a socioeconomic factor[3]. Some other studies explained that poor nutritional status poses 2.216 times[10], 2.17 times[15] and 1.2 times[12] greater risk of diphtheria as opposed to good nutritional status.

In recent decades, there has been a shift in the age group of diphtheria patients, from <5 year-old to >15 year-old and adult[5]. This may correlate with the vaccination program for children in the vast majority of the countries in the world[5]. This study determines the age limit of an individual being at risk of diphtheria to over 19 years old. Such limit is based on a span of 10 years from the last Td (tetanus-diphtheria) vaccination program. Td vaccination in Indonesia is conducted in year 2 or 3 of elementary school, which is at the age of 8 or 9 years old. When an individual has received vaccines for complete immunization including Td, he/she would be protected for up to 18 – 19 years of age. Individuals with a risky age have 12 times more chances of suffering from diphtheria compared to those whose age status is not as risky. Research in Bangkalan district concluded that 74% of diphtheria cases occurred in the age group of >15 year-old[18].

The association between age and diphtheria cases can be linked to the diphtheria antibody titer within the body[19]. The older the age, the lower the titer will become, but it will return to a higher level after booster vaccination[19], [20].

Such vaccination has to be performed since the anti-diphtheria serological titer at the age of 14-15 has no significant effects and provides less function of protection[17].

Immunization status is the key factor linked to diphtheria with $OR = 0.044$, thus indicating that incomplete immunization status poses 22.72 ($1/0.044$) times greater risk of individuals contracting diphtheria compared to complete immunization along with the control by another variable. The secondary data and direct interviews revealed that the problem of the society members who are unvaccinated or with incomplete vaccination mainly comes from the mothers having a lack of knowledge or information on immunization. Other facts linked to the low immunization coverage are low socioeconomic status and misinformation about immunization. Previous studies have proved that the mother's knowledge has a significant correlation with diphtheria incidence [9], [10], [21].

Families with low socioeconomic status tend to live in a slump area or do not fulfill the requirements of healthy environment [5]. The environment correlates with diphtheria incidence[22]. A poor environment has 4.27 times greater risk of diphtheria compared to a healthy environment[22].

Another reason for unvaccinated individuals is misinformation about immunization. This is derived from the false perception developed in *pesantren* (Islamic boarding school) in Cirebon which considers vaccines as containing illicit substances that should not therefore enter the body. However, the diphtheria outbreak in the community has facilitated Cirebon Health Office to disseminate information on immunization, particularly to religious leaders. Furthermore, the Indonesian Ulema Council has officially issued a fatwa on immunization[23] which stated that, first, immunization is strongly recommended for the sake of health, and it can even be categorized as mandatory when referring to *sadd adz-dzari'ah*. Second, according to *istihlak*, immunization with a mixture of allegedly illicit substances becomes halal when the vaccine has been washed with chemicals. Lastly, if there are indications of haram (forbidden by the Islamic law), then it remains to be allowed for emergency measures and protection from harm.

5. CONCLUSION

The factors that correlate with diphtheria include vaccination status, age, and transmission source, with the vaccination status becoming the most dominant factor.

Other factors probably linked to diphtheria are mother's knowledge, economic status, and misinformation.

ACKNOWLEDGMENT

The author would like to thank the Medical Faculty of Universitas Islam Indonesia, Cirebon Office of Health, and Gunung Jati Public Hospital Cirebon for the support in this study.

REFERENCES

- [1] Centers for Disease Control and Prevention, "About Diphtheria," 2016.
- [2] National Foundation for Infectious Disease, "Fact About Diphtheria for Adult," 2008.
- [3] K. Sariatji, N. E. Pracoyo, and R. H. Putranto, "Epidemiologi Kasus Difteri di Kabupaten Lebak Provinsi Banten Tahun 2014," *Media Litbangkes*, vol. 26, pp. 37–44, 2016, doi: 10.22435/mpk.v26i1.4902.37-44.
- [4] Ikatan Dokter Indonesia, "KLB Difteri Indonesia Terbesar di Dunia," 2017.
- [5] K. E. N. Clarke, "Review of the Epidemiology of Diphtheria - 2000 - 2016," 2016.
- [6] Kementerian Kesehatan Republik Indonesia, "Pemerintah Optimis KLB Difteri Bisa Teratasi," 2018.
- [7] Dinas Kesehatan Kabupaten Cirebon, *Profil Kesehatan Kabupaten Cirebon 2017*. Cirebon, 2018.
- [8] B. Basuki, *Aplikasi Metode Kasus-Kontrol*. Jakarta, Indonesia: Ilmu Kedokteran Komunitas, Fakultas Kedokteran Universitas Indonesia, 2002.
- [9] B. Kartono, "Lingkungan Rumah dan Kejadian Difteri di Kabupaten Tasikmalaya dan Kabupaten Garut," *Kesmas-National Public Heal. J.*, vol. 2, no. 5, pp. 200–204, 2008.
- [10] K. S. Lestari, "Faktor-Faktor yang Berhubungan Dengan Kejadian Difteri di Kabupaten Sidoarjo," Univeritas Indonesia, 2012.
- [11] I. F. Arifin and C. I. Prasasti, "Factors That Related with Diphtheria Cases of Children in Bangkalan Health Centers in 2016," *J. Berk. Epidemiol.*, vol. 5, no. 1, pp. 26–36, 2017, doi: 10.20473/jbe.v5i1.2017.26-36.
- [12] R. V. Sitohang, "Hubungan kepadatan serumah dengan kejadian difteri pada kejadian luar biasa (KLB) difteri di kabupaten Cianjur Jawa Barat tahun 2000 - 2001," Universitas Indonesia, 2002.
- [13] N. Izza and Soenarnatalina, "Analysis of Spatial Data of Diphtheria Disease in East Java Province during the year 2010 and 2011," *Bul. Penelit. Sist. Kesehat.*, vol. 18, no. 2, pp. 211–219, 2015.
- [14] A. W. Utami, "Faktor yang Mempengaruhi Kejadian Penularan Difteri di Kota Blitar Propinsi Jawa Timur," Universitas Airlangga Surabaya, 2010.
- [15] Rusli, "Hubungan Status Imunisasi Difteri dengan Kejadian Difteri Pada Kejadian Luar Biasa (KLB) di Kabupaten Cianjur tahun 2001," Universitas Indonesia Jakarta, 2003.
- [16] Dinas Kesehatan Provinsi Jawa Barat, "Profil Kesehatan Provinsi Jawa Barat Tahun 2016," Bandung - Jawa Barat, 2017.
- [17] K. Rusmil, A. Chairulfatah, E. Fadlyana, and M. Dhamayanti, "Wabah Difteri di Kecamatan Cikalong Wetan, Kabupaten Cianjur, Jawa Barat, Indonesia," *Sari Pediatr.*, vol. 12, no. 6, pp. 397–403, 2011.
- [18] S. D. Sari, "Penyelidikan Epidemiologi KLB Difteri Di Kecamatan Tanjung Bumi Kabupaten Bangkalan," *Str. J. Ilm. Kesehat.*, vol. 2, no. 1, 2012.
- [19] U. Kunarti, "The Diphtheria G Immunoglobulin Titer in School Children. Case Study in Kota Semarang," Universitas Diponegoro Semarang, 2004.
- [20] I. H. Al Aswad and M. E. Shubair, "Efficacy of diphtheria and tetanus vaccination in Gaza, Palestine," *East. Mediterr. Heal. J.*, vol. 15, no. 2, 2009.
- [21] G. Alfiansyah, "Epidemiological Investigation of Diphtheria's Outbreak at Blitar District in 2015," *Preventia*, vol. 2, no. 1, 2017.
- [22] Al. B. G. Lia, "Faktor Resiko Kejadian Difteri Pada KLB Difteri di Sidoarjo Tahun 2010," Universitas Airlangga Surabaya, 2010.
- [23] M. Munajat, "Imunisasi Menurut Kajian MUI," in *Seminar Nasional Imunisasi*, 2017, vol. 2017.